



## CLAIMS

1. A recombinant gene medicine of adenovirus vector and p53 gene for treating proliferative disease, wherein it is constructed by adenovirus vector and human tumor suppressor p53 gene expression cassette, and its recombinant sequence is:

the right end of adenovirus 5 -

ATGTTTACCGCCACACTCGCAGGGTCTGCACCTGGTGCGGGTCTCATCGTAC  
CTCAGCACCTTCCAGATC<sub>70</sub>TCTGACATGCGATGTCGACTCGACTGCTTCGCG  
ATGTACGGGGCCAGATATACGCGTATCTGAGGGGACTAGGGTGTGTTTAGGCG  
10 AAAAGCGGGGCTTCGGTTGTACGCGGTTAGGAGTCCCCTCAGGATATAGTAG  
TTTCGCTTTTGCATAGGGAGGGGGAAATGTAGTCTTATGCAATACTCTTGTA  
TCTTGCAACATGGTAACGATGAGTTAGCAACATGCCTTACAAGGAGAGAAAA  
GCACCGTGATGCCGATTGGTGAAGTAAGGTGGTACGATCGTGCCTTATTA  
GGAAGGCAACAGACGGGTCTGACATGGATTGGACGAACCACTGAATTCCGCA  
15 TTGCAGAGATATTGTATTTAAGTGCCTAGCTCGATACAATAAACGCCATTTGAC  
CATTACCACATTGGTGTGCACCTCCAAGCTTGGTACCGAGCTCGGATCCCG<sub>5</sub>  
23CTAGAGCCACCGTCCAGGGAGCAGGTAGCTGCTGGGCTCCGGGGACACTT  
TGCGTTCGGGCTGGGAGCGTCTTTCCACGACGGTGACACGCTTCCCTGGATT  
GGCAGCCAGACTGCTTTCCGGGTCACTGCC<sub>655</sub>ATGGAGGAGCCGCAGTCAGA  
20 TCCTAGCGTCGAGCCCCCTCTGAGTCAGGAAACATTTTCAGACCTATGGAAAC  
TACTTCCTGAAAACAACGTTCTGTCCCCCTTGCCGTCCCAAGCAATGGATGAT  
TTGATGCTGTCCCCGGACGATATTGAACAATGGTTCACTGAAGACCCAGGTC  
CAGATGAAGCTCCCAAGATGCCAGAGGCTGCTCCCCCGTGGCCCCCTGCAC  
CAGCAGCTCCTACACCGGCGGGCCCCCTGCACCAGCCCCCTCCTGGCCCCCTGT  
25 CATCTTCTGTCCCTTCCCAGAAAACCTACCAGGGCAGCTACGGTTTCCGTCTG  
GGCTTCTTGCACTTCTGGGACAGCCAAGTCTGTGACTTGACGTACTCCCCTG  
CCCTCAACAAGATGTTTTGCCAACTGGCCAAGACCTGCCCTGTGCAGCTGTG  
GGTTGATTCCACACCCCCGCCCCGGCACCCGCGTCCGCGCCATGGCCATCTA  
CAAGCAGTCACAGCACATGACGGAGGTTGTGAGGCGCTGCCCCCACCATGA  
30 GCGCTGCTCAGATAGCGATGGTCTGGCCCCCTCCTCAGCATCTTATCCGAGTG  
GAAGGAAATTTGCGTGTGGAGTATTTGGATGACAGAAACACTTTTCGACATAG  
TGTGGTGGTGCCCTATGAGCCGCCTGAGGTTGGCTCTGACTGTACCACCATC  
CACTACAACATACATGTGTAACAGTTCCTGCATGGGCGGCATGAACCGGAGGC  
CCATCCTCACCATCATCACACTGGAAGACTCCAGTGGTAATCTACTGGGACG  
35 GAACAGCTTTGAGGTGCGTGTTTGTGCCTGTCCTGGGAGAGACCGGCGCACA  
GAGGAAGAGAATCTCCGCAAGAAAGGGGAGCCTCACCACGAGCTGCCCCCA  
GGGAGCACTAAGCGAGCACTGCCCAACAACACCAGCTCCTCTCCCCAGCCAA  
AGAAGAAACCACTGGATGGAGAATATTTACCCTTCAGATCCGTGGGCGTGA  
GCGCTTCGAGATGTTCCGAGAGCTGAATGAGGCCTTGGAACCTCAAGGATGCC  
40 CAGGCTGGGAAGGAGCCAGGGGGGAGCAGGGCTCACTCCAGCCACCTGAA  
GTCCAAAAAGGGTCAGTCTACCTCCCGCCATAAAAACTCATGTTCAAGACAG  
AAGGGCCTGACTCAGACTGA<sub>1837</sub>CATTCTCCACTTCTTGTTCCCCACTGACAGC  
CTCCACCCCCATCTCTCCCTCCCCTGCCATTTTGGGTTTTGGGTCTTTGAAC

CCTTGCTTGCAATAGGTGTGCGTCAGAAGCACCCAGGACTTCCATTTGCTTTG  
 TCCCGGGGCTCCACTGAACAAGTTGGCCTGCACTGGTGTGTTTGTGTTGGGGA  
 GGAGGATGGGGAGTAGGACATAACCAGCTTAGATTTTAAGGTTTTTACTGTGAG  
 GGATGTTTGGGAGATGTAAGAAATGTTCTTGCAAGTTAAGGGTTAGTTTACAAT  
 5 CAGCCACATTCTAGGTAGGGGGCCACTTCACCGTACTAACCAGGGAAGCTGTC  
 CCTCACTGTTGAATTTTCTCTAACTTCAAGGCCCATATCTGTGAAATGCTGGAT  
 TTGCCCTACCTCGGAATGCTGGCATTGTCACCTACCTCACAGAGTGCATTGTG  
 AGGGTT<sup>2297</sup>AATGAAATAATGTACATCTGGCCTTGAAACCACCTTTTATTACATG  
 GGGTCTAGCGGGATCCACTAGTAACGCCGCCAGTGTGCTGGAATTCTGCAGA  
 10 TATCCATCACACTGGCGGCCGCTCGAGCATGCATCTAGAGCTCGCTGATCAG  
 CCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGGCCCTCCCCCGTG  
 CCTTCCTTGACCCTGGAAGGTGCCACTCCCCTGTCCTTTCCTAATAAAATGA  
 GGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGG  
 GTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCT  
 15 GGGGATGCGGTGGGCTCTATGGCTTCTGAGGCGGAAAGAACCAGCTGGGGC  
 TCGAGGGGGATCCCCACGCTAGAGCT<sup>2733</sup>GACTATAATAATAAAACGCCAACT  
 TTGACCCGGAACGCGGAAAACACCTGAGAAAAACACCTGGGCGAGTCTCCAC  
 GTAAACGGTCAAAGTCCCCGCGGCCCTAGACAAATATTA<sup>2848</sup>- the left end of  
 adenovirus 5,

wherein:

- 1) the right end of adenovirus 5 and the left end of adenovirus 5 are described in the full sequence of adenovirus 5 (Genbank No: NC\_001406)
- 2) 1-70: the right arm of adenovirus (the 70<sup>th</sup> base locates at adenovirus gene sequence 3328)
- 25 3) 71-523 Rous Sarcoma Virus (RSV) LTR (promoter)
- 4) 524-655: 5' end non-translating region
- 5) 656-1837: p53 gene coding sequence
- 6) 1838-2733: 3' end non-translating region (poly Adenosine tail starting at 2298)
- 2734-2848: the left arm of adenovirus (base at 2734 is positioned at 452 of
- 30 adenovirus 5 gene sequence).

2. The recombinant gene medicine according to Claim 1, wherein the gene expression cassette of the recombinant is a specific sequence composed of promoter-p53cDNA-poly adenosine.

3. The recombinant gene medicine according to claim 2, wherein the upstream of the gene expression cassette is any eukaryotic cell promoters, prokaryotic cell promoters or virus promoters, and the downstream is any of the eukaryotic gene poly adenosine residues (Poly A tail).

4. The recombinant gene medicine according to claim 1, wherein the recombinant gene medicine is obtained in prokaryotic cells by homologous recombination, including:

- 1) the recombinant pGT-2 is obtained by homologous recombination of adenovirus and plasmid pGT-1 (containing two inverted terminal repeats on both ends of adenovirus) in *E. coli*;
- 2) the recombinant pGT-3 is obtained by homologous recombination of pGT-2 and artificial sequence "the right arm of adenovirus/ promoter-p53cDNA-poly A / the left arm of adenovirus " in *E. coli*;
- 3) The recombinant p53 adenovirus is obtained by discarding the prokaryotic sequence using endonuclease *Pacl*.
5. The recombinant gene medicine according to claim 4, wherein the recombinant gene medicine is obtained in any prokaryotic cells by homologous recombination.
6. The recombinant gene medicine according to claim 1 is used to produce injection solution.
7. The recombinant gene medicine according to claim 6 is used to produce injection.